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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION of
Ibrahim, et al.

Group Art Unit: 1655

Serial No.: 09/444,095

Examiner: Sisson, B.

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FOR: Purification Method and Apparatus

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Declaration Under 37 C.F.R. **1.132**

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

1. I, M. Sofi Ibrahim am an inventor of the above identified application.
2. I am employed by United States Army Medical Research Institute of Infectious Diseases.
3. I hold the title of Microbiologist.
4. I have the following degrees from the following institutions_B.Sc., Ain Shams University, Cairo, Egypt; M.Sc., Ain Shams University, Cairo, Egypt; Ph.D. Johns Hopkins University, Baltimore, MD.
5. My area of expertise is in Molecular Biology.
6. The term "deep reactive ion etchings is a term that is well known in the art as evidenced by the attached exhibit entitled "Microfabricated filters for microfluidic analytical systems" by B. He, L. Tan and F. Regnier published in Analytical Chemistry April 1, 1999, volume 71, part 7, pages: 1464-1468.

7. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statement and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title

Ibrahim
Serial No. 09/444,095

18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

Dated: June 26, 2002.

Mohamed Sofi Ibrahim

M. Sofi Ibrahim

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Microfabricated Filters for Microfluidic Analytical Systems

Bing He, Li Tan, and Fred Regnier*

Department of Chemistry, Purdue University, Lafayette, Indiana 47907

Solvent and reagent filters were micromachined into quartz wafers using deep reactive ion etching to create a network of intersecting 1.5 × 10 μm channels. When placed at the bottom of reservoirs with a side exit, this channel network behaved as a lateral percolation filter composed of an array of cubelike structures one layer deep. Flow through these filters was driven by electroosmotic flow (EOF). Silanol groups at the walls of channels in the network provided the requisite charge to trigger EOF when voltage was applied laterally to the filter. Adsorption of cationic proteins in this silanol-rich matrix was controlled by the application of a polyacrylamide coating prepared by bonding *N*-hydroxysuccinimide (NHS)-activated poly(acrylic acid) to (γ-aminopropyl)silane-derivatized filters. Subsequent reaction of residual NHS groups in the coating with 2-(2-aminoethoxy)ethanol provided channels of low charge density and adsorptivity. These lateral percolation filters were shown to be efficacious in filtering solvents containing a variety of particulate materials, ranging from dust to cells.

The need to analyze increasingly smaller samples has stimulated great interest in microtechnology. Affinity biodot arrays on planar surfaces,[1,2] microfabricated reaction vessels,[3] capillary liquid chromatography and electrophoresis columns,[4,5] and a variety of sensors ranging from microelectrochemical[6] and surface plasmon resonance-based devices to those exploiting a medley of waveguide technologies[7–9] are all examples of efforts to accommodate smaller samples by miniaturization.

An even more aggressive approach is to miniaturize and integrate all the components of the analytical system in a microchannel network where sample preparation, sampling, chemical reactions, separations, and detection are achieved in a single device.[10,11] Among the more appealing features of this strategy are that (i) all the unit operations are integrated, (ii) reagent consumption will be very low, (iii) sample volume will be small, (iv) analyte recovery would be maximized, (v) contamination would be minimized, and (vi) many systems could be fabricated and operated in parallel. For this concept to be realized on a wide scale, it will be necessary to miniaturize the whole analytical system. This paper examines the issue of filtration in these microfluidic systems.

At present, lithographic,[12] embossing, and casting processes using a micromachined mask or molds[13,14] are the dominant technologies used to create the 1–100-μm objects and channels on which these integrated systems are based. The fact that microchannels of less than 20–30 μm are easily blocked by particles is a problem. These particles may be transported into the system in solvents, crystallize from samples while they are being held in reservoirs on chips, or arise from microbial growth in buffers during storage. Prefiltration would be helpful, but conventional filtration techniques require orders of magnitude greater volumes than used in sample and solvent reservoirs on chips. This approach also fails to address on-chip particulate formation. Microfiltration within the device would be a much better solution.

Microfabricated filters have been described for trapping different cell types from blood,[15] but the objective was to harvest cells, not prepare particle-free solvents and samples. These filters were made by microfabricating arrays of rectangular, parallel channels on chips of a width and height that would not allow particles larger than the channels to enter the channel network along the axis parallel to the chip surface. This type of filter is similar to the frited glass or membrane filter devices widely used in laboratories to harvest particulate materials. Filtration of this type will be referred to as *axial percolation* filtration because it occurs by percolating liquid through a filter bed along the flow axis. Axial percolation filters are generally of high cross-sectional area at the point of filtration to provide many parallel channels

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